	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L1	202	beta-catenin	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/08/20 16:18			0
2	BRS	L2	7943	lef-1 or tcf-4 or apc or conductin or e-cadherin	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/08/20 16:18			0
3	BRS	L3	7943	transcription adj factor	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/08/20 16:18			0
4	BRS	L4	214	tumor adj suppressor adj gene adj product	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/08/20 16:19			0
5	BRS	L5	109	1 same (2 or 3 or 4)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/08/20 16:20			0
6	BRS	L6	34	1 same (2 or 3 or 4) same interact$3	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/08/20 16:20			0

=> d his

(FILE 'HOME' ENTERED AT 16:34:25 ON 20 AUG 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
16:34:59 ON 20 AUG 2002
L1 13370 S (BETA-CATENIN) OR (BETA CATENIN)
L2 55552 S LEF-1 OR TCF-4 OR APC OR CONDUCTIN OR E-CADHERIN
L3 294851 S TRANSCRIPTION FACTOR
L4 2000 S TUMOR SUPPRESSOR GENE PRODUCT
L5 6498 S L1 (P) (L2 OR L3 OR L4)
L6 1670 S L5 (P) INTERACT?
L7 75 S L6 (P) (COMPOUND OR AGENT OR SUBSTANCE OR COMPOSITION)
L8 22 DUPLICATE REMOVE L7 (53 DUPLICATES REMOVED)
L9 12 S L8 (P) (AFFECT? OR INHIBIT? OR PROMOT?)

=> log y

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FILE 'HOME' ENTERED AT 16:34:25 ON 20 AUG 2002

=> file medline caplus biosis embase scisearch agricola
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'MEDLINE' ENTERED AT 16:34:59 ON 20 AUG 2002

FILE 'CAPLUS' ENTERED AT 16:34:59 ON 20 AUG 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE 'AGRICOLA' ENTERED AT 16:34:59 ON 20 AUG 2002

=> s beta?catenin
'?' TRUNCATION SYMBOL NOT VALID WITHIN 'BETA?CATENIN'
'?' TRUNCATION SYMBOL NOT VALID WITHIN 'BETA?CATENIN'
'?' TRUNCATION SYMBOL NOT VALID WITHIN 'BETA?CATENIN'
'?' TRUNCATION SYMBOL NOT VALID WITHIN 'BETA?CATENIN'
'?' TRUNCATION SYMBOL NOT VALID WITHIN 'BETA?CATENIN'
'?' TRUNCATION SYMBOL NOT VALID WITHIN 'BETA?CATENIN'
The truncation symbol ?  may be used only at the end of a search
term.  To specify a variable character within a word use '!', e.g.,
'wom!n' to search for both 'woman' and 'women'.  Enter "HELP
TRUNCATION" at an arrow prompt (=>) for more information.

=> s (beta-catenin) or (beta catenin)
L1       13370 (BETA-CATENIN) OR (BETA CATENIN)

=> s LEF-1 or TCF-4 or APC or conductin or e-cadherin
L2       55552 LEF-1 OR TCF-4 OR APC OR CONDUCTIN OR E-CADHERIN

=> s transcription factor
L3      294851 TRANSCRIPTION FACTOR

=> s tumor suppressor gene product
L4        2000 TUMOR SUPPRESSOR GENE PRODUCT

=> s l1 (p) (l2 or l3 or l4)
L5        6498 L1 (P) (L2 OR L3 OR L4)

=> S L5 (P) INTERACT?
L6        1670 L5 (P) INTERACT?

=> S L6 (P) (COMPOUND OR agent or substance or composition)
   5 FILES SEARCHED...
L7          75 L6 (P) (COMPOUND OR AGENT OR SUBSTANCE OR COMPOSITION)

=> duplicate remove l7
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L7
L8           22 DUPLICATE REMOVE L7 (53 DUPLICATES REMOVED)

=> d l8 1-22 ibib abs

L8   ANSWER 1 OF 22     MEDLINE                          DUPLICATE 1
ACCESSION NUMBER:   2002221111     MEDLINE
DOCUMENT NUMBER:    21957086   PubMed ID: 11960376
```

TITLE: UCS15A, a novel small molecule, SH3 domain-mediated protein-protein interaction blocking drug.
AUTHOR: Oneyama Chitose; Nakano Hirofumi; Sharma Sreenath V
CORPORATE SOURCE: Tokyo Research Laboratories, Kyowa Hakko Kogyo Co., Ltd 3-6-6 Asahi-cho, Machida-shi, Tokyo 194, Japan.
SOURCE: ONCOGENE, (2002 Mar 27) 21 (13) 2037-50.
Journal code: 8711562. ISSN: 0950-9232.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020418
Last Updated on STN: 20020511
Entered Medline: 20020510

AB Protein-protein ***interactions*** play critical regulatory roles in mediating signal transduction. Previous studies have identified an unconventional, small-molecule, Src signal transduction inhibitor, UCS15A. UCS15A differed from conventional Src-inhibitors in that it did not alter the levels or the tyrosine kinase activity of Src. Our studies suggested that UCS15A exerted its Src-inhibitory effects by a novel mechanism that involved the disruption of protein-protein ***interactions*** mediated by Src. In the present study we have examined the ability of UCS15A to disrupt the ***interaction*** of Src-SH3 with Sam68, both in vivo and in vitro. This ability of UCS15A was not restricted to Src-SH3 mediated protein-protein ***interactions*** , since the drug was capable of disrupting the in vivo ***interactions*** of Sam68 with other SH3 domain containing proteins such as Grb2 and PLCgamma. In addition, UCS15A was capable of disrupting other typical SH3-mediated protein-protein ***interactions*** such as Grb2-Sos1, cortactin-ZO1, as well as atypical SH3-mediated protein-protein ***interactions*** such as Grb2-Gab1. However, UCS15A was unable to disrupt the non-SH3-mediated protein-protein ***interactions*** of ***beta*** - ***catenin*** , with ***E*** - ***cadherin*** and alpha-catenin. In addition, UCS15A had no effect on the SH2-mediated ***interaction*** between Grb2 and activated Epidermal Growth Factor receptor. Thus, the ability of UCS15A, to disrupt protein-protein ***interactions*** appeared to be restricted to SH3-mediated protein-protein ***interactions*** . In this regard, UCS15A represents the first example of a non-peptide, small molecule ***agent*** capable of disrupting SH3-mediated protein-protein ***interactions*** . In vitro analyses suggested that UCS15A did not bind to the SH3 domain itself but rather may ***interact*** directly with the target proline-rich domains.

L8 ANSWER 2 OF 22 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2002124710 MEDLINE
DOCUMENT NUMBER: 21828326 PubMed ID: 11839557
TITLE: Beta-catenin--a linchpin in colorectal carcinogenesis?.
AUTHOR: Wong Newton Alexander Chiang Shuek; Pignatelli Massimo
CORPORATE SOURCE: Department of Pathology, University of Edinburgh, Edinburgh, Scotland, United Kingdom.
SOURCE: AMERICAN JOURNAL OF PATHOLOGY, (2002 Feb) 160 (2) 389-401.
Ref: 140
Journal code: 0370502. ISSN: 0002-9440.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20020226
Last Updated on STN: 20020320
Entered Medline: 20020319

AB An important role for ***beta*** - ***catenin*** pathways in colorectal carcinogenesis was first suggested by the protein's association with adenomatous polyposis coli (***APC***) protein, and by evidence of dysregulation of ***beta*** - ***catenin*** protein expression at all stages of the adenoma-carcinoma sequence. Recent studies have, however, shown that yet more components of colorectal carcinogenesis are linked to ***beta*** - ***catenin*** pathways. Pro-oncogenic factors that also release ***beta*** - ***catenin*** from the adherens

complex and/or encourage translocation to the nucleus include ras, epidermal growth factor (EGF) [redacted]-erbB-2, PKC-betaII, MUC1, and [redacted]AR-gamma, whereas anti-oncogenic factors that also inhibit nuclear ***beta*** - ***catenin*** signaling include transforming growth factor (TGF)-beta, retinoic acid, and vitamin D. Association of nuclear ***beta*** - ***catenin*** with the T cell factor (TCF)/lymphoid enhancer factor (LEF) family of ***transcription*** ***factors*** promotes the expression of several ***compounds*** that have important roles in the development and progression of colorectal carcinoma, namely: c-myc, cyclin D1, gastrin, cyclooxygenase (COX)-2, matrix metalloproteinase (MMP)-7, urokinase-type plasminogen activator receptor (aPAR), CD44 proteins, and P-glycoprotein. Finally, genetic aberrations of several components of the ***beta*** - ***catenin*** pathways, eg, Frizzled (Frz), AXIN, and ***TCF*** - ***4*** , may potentially contribute to colorectal carcinogenesis. In discussing the above ***interactions*** , this review demonstrates that ***beta*** - ***catenin*** represents a key molecule in the development of colorectal carcinoma.

L8 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:661652 CAPLUS
DOCUMENT NUMBER: 135:207457
TITLE: Modulation of pleiotrophin signaling by receptor-type protein tyrosine phosphatase .beta./.zeta. and therapeutic use
INVENTOR(S): Deuel, Thomas
PATENT ASSIGNEE(S): Barnes-Jewish Hospital, USA
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001064944	A1	20010907	WO 2001-US6476	20010228

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-185653P P 20000229
AB The mechanism by which pleiotrophin binds to the protein tyrosine phosphatase .zeta./receptor-like protein tyrosine phosphatase .beta. (RPTP .beta./.zeta.) is disclosed along with methods of modulating both pleiotrophin expression and signaling to treat, prevent and inhibit abnormal cell growth states. Applicants have shown that RPTP .beta./.zeta. is the receptor for pleiotrophin. Binding of RPTP .beta./.zeta. and pleiotrophin inhibits RPTP .beta./.zeta. enzymic activity and results in higher levels of tyrosine phosphorylation of . ***beta*** .- ***catenin*** . Further, binding of RPTP .beta./.zeta. and pleiotrophin also reduces the levels of . ***beta*** .- ***catenin*** ***interaction*** with ***E*** - ***cadherin*** and thus affects the potential for cells to adhere with each other. The elucidation of this relationship between RPTP .beta./.zeta. and pleiotrophin can be used to define ***compds*** . useful in therapy and treating disease. Specifically provided are methods of inhibiting tumor growth, promotion, metastasis, invasiveness and angiogenesis as well as methods of preventing or inhibiting cell adhesion.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:168023 CAPLUS
DOCUMENT NUMBER: 134:202688
TITLE: .beta.-Catenin, transcription factor Tcf-4, and APC gene interact to prevent cancer
INVENTOR(S): Barker, Nicholas; Clevers, Johannes C.; Kinzler,

Kenneth W[redacted] Korinek, Vladimir; Morin, Patrice J.; Sparks, A[redacted]rew B.; Vogelstein, Bert; He, T[redacted]-Chuan
PATENT ASSIGNEE(S): The Johns Hopkins University, USA
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001016167	A2	20010308	WO 2000-US23635	20000829
WO 2001016167	A3	20010920		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-388354 A1 19990901

AB A recombinant adenovirus (Ad-Mini-ME) which constitutively expresses the central third of APC includes all of the known .beta.-catenin binding repeats. When expressed in colon cancer cells, Ad-Mini-ME blocked the nuclear translocation of .beta.-catenin and inhibited .beta.-catenin/Tcf-4-mediated transactivation. Accordingly, expression of endogenous targets of the APC/.beta.-catenin/Tcf-4 pathway were down-regulated. Ad-Mini-ME infection of colorectal cancer cell lines with mutant APC but wild-type .beta.-catenin resulted in substantial growth arrest followed by apoptosis. Also disclosed are protein and cDNA sequences of human transcription factor Tcf-4. These findings suggest that the .beta.-catenin binding domain in the central third of APC is sufficient for its tumor suppression activity.

L8 ANSWER 5 OF 22 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2001640069 MEDLINE
DOCUMENT NUMBER: 21548408 PubMed ID: 11689703
TITLE: Cell density and phosphorylation control the subcellular localization of adenomatous polyposis coli protein.
AUTHOR: Zhang F; White R L; Neufeld K L
CORPORATE SOURCE: Department of Oncological Sciences, University of Utah, Salt Lake City, Utah 84112, USA.
CONTRACT NUMBER: 5PO1 CA73992-02 (NCI)
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (2001 Dec) 21 (23) 8143-56. Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011107
Last Updated on STN: 20020123
Entered Medline: 20011205

AB Loss of functional adenomatous polyposis coli protein (***APC***) leads to uncontrolled proliferation of colonic epithelial cells, as evidenced by polyp formation, a prelude to carcinogenesis. As a tumor suppressor, ***APC*** targets the oncogene ***beta*** - ***catenin*** for proteasome-mediated cytoplasmic degradation. Recently, it was demonstrated that ***APC*** also ***interacts*** with nuclear ***beta*** - ***catenin*** , thereby reducing ***beta*** - ***catenin*** 's activity as a transcription cofactor and enhancing its nuclear export. The first objective of this study was to analyze how cellular context affected ***APC*** distribution. We determined that cell density but not cell cycle influenced ***APC*** 's subcellular distribution, with predominantly nuclear ***APC*** found in subconfluent MDCK and intestinal epithelial cells but both cytoplasmic and nuclear ***APC*** in superconfluent cells. Redistribution of ***APC*** protein did not depend on continual nuclear export. Focusing on the two defined nuclear localization signals in the C-terminal third of

APC (NLS1(***APC***) and NLS2(***APC***)), we found that phosphorylation at the CK2 si[redacted] increased and phosphorylation [redacted] the PKA site decreased NLS2(***APC***)-mediated nuclear translocation. Cell density-mediated redistribution of beta-galactosidase was achieved by fusion to NLS2(***APC***) but not to NLS1(***APC***). Both the CK2 and PKA sites were important for this density-mediated redistribution, and pharmacological ***agents*** that target CK2 and PKA instigated relocalization of endogenous ***APC*** . Our data provide evidence that physiological signals such as cell density regulate ***APC*** 's nuclear distribution, with phosphorylation sites near NLS2(***APC***) being critical for this regulation.

L8 ANSWER 6 OF 22 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2001640546 MEDLINE
DOCUMENT NUMBER: 21548943 PubMed ID: 11691822
TITLE: Human APC2 localization and allelic imbalance.
AUTHOR: Jarrett C R; Blancato J; Cao T; Bressette D S; Cepeda M; Young P E; King C R; Byers S W
CORPORATE SOURCE: The Lombardi Cancer Research Center, Georgetown University School of Medicine, Washington, DC 20007, USA.
CONTRACT NUMBER: R21 CA87749 (NCI)
SOURCE: CANCER RESEARCH, (2001 Nov 1) 61 (21) 7978-84.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011107
Last Updated on STN: 20020123
Entered Medline: 20011204

AB A second adenomatous polyposis coli (***APC***)-like gene, APC2/APCL, was recently described and localized to chromosome 19. We have fine mapped APC2 to a small region of chromosome 19p13.3 containing markers D19S883 and WI-19632, a region commonly lost in a variety of cancers, particularly ovarian cancer. Interphase fluorescence in situ hybridization analysis revealed an APC2 allelic imbalance in 19 of 20 ovarian cancers screened and indicates that APC2 could be a potential tumor suppressor gene in ovarian cancer. When overexpressed in SKOV3 ovarian cancer cells, which express low levels of APC2, exogenous APC2 localized to the Golgi apparatus, actin-containing structures, and occasionally to microtubules. Antibodies against the NH2 terminus of human APC2 show that endogenous APC2 is diffusely distributed in the cytoplasm and colocalizes with both the Golgi apparatus and actin filaments. APC2 remained associated with actin filaments after treatment with the actin-disrupting ***agent*** , cytochalasin D. These results suggest that APC2 is involved in actin-associated events and could influence cell motility or adhesion through ***interaction*** with actin filaments, as well as functioning independently or in cooperation with ***APC*** to down-regulate ***beta*** - ***catenin*** signaling.

L8 ANSWER 7 OF 22 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 2002003046 MEDLINE
DOCUMENT NUMBER: 21623063 PubMed ID: 11751639
TITLE: Chromatin-specific regulation of LEF-1-beta-catenin transcription activation and inhibition in vitro.
AUTHOR: Tutter A V; Fryer C J; Jones K A
CORPORATE SOURCE: Regulatory Biology Laboratory, The Salk Institute for Biological Studies, La Jolla, California 92037, USA.
SOURCE: GENES AND DEVELOPMENT, (2001 Dec 15) 15 (24) 3342-54.
Journal code: 8711660. ISSN: 0890-9369.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20020102
Last Updated on STN: 20020125
Entered Medline: 20020122

AB Transcriptional activation of Wnt/Wg-responsive genes requires the stabilization and nuclear accumulation of ***beta*** - ***catenin*** , a dedicated coactivator of LEF/TCF enhancer-binding proteins. Here we

report that recombinant ***beta*** - ***catenin*** strongly enhances binding and transactivation by ***LEF*** - ***1*** on chromatin templates in vitro. Interestingly, different ***LEF*** - ***1*** isoforms vary in their ability to bind nucleosomal templates in the absence of ***beta*** - ***catenin*** , owing to N-terminal residues that repress binding to chromatin, but not nonchromatin, templates. Transcriptional activation in vitro requires both the armadillo (ARM) repeats and the C terminus of ***beta*** - ***catenin*** , whereas the phosphorylated N terminus is inhibitory to transcription. A fragment spanning the C terminus (CT) and ARM repeats 11 and 12 (CT-ARM), but not the CT alone, functions as a dominant negative inhibitor of ***LEF*** - ***1*** -beta-cat activity in vitro and can block ATP-dependent binding of the complex to chromatin. ***LEF*** - ***1*** -beta-cat transactivation in vitro was also repressed by inhibitor of ***beta*** - ***catenin*** and ***Tcf*** - ***4*** (ICAT), a physiological inhibitor of Wnt/Wg signaling that ***interacts*** with ARM repeats 11 and 12, and by the nonsteroidal anti-inflammatory ***compound*** , sulindac. None of these transcription inhibitors (CT-ARM, ICAT, or sulindac) could disrupt the ***LEF*** - ***1*** -beta-cat complex after it was stably bound to chromatin. We conclude that the CT-ARM region of ***beta*** - ***catenin*** functions as a chromatin-specific activation domain, and that several inhibitors of the Wnt/Wg pathway directly modulate ***LEF*** - ***1*** -beta-cat activity on chromatin.

L8 ANSWER 8 OF 22 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 2001649600 MEDLINE
DOCUMENT NUMBER: 21558943 PubMed ID: 11701326
TITLE: beta-catenin: molecular plasticity and drug design.
AUTHOR: Daniels D L; Eklof Spink K; Weis W I
CORPORATE SOURCE: Dept of Structural Biology, Stanford University School of Medicine 299 Campus Dr., West Stanford, CA 94305, USA.
SOURCE: TRENDS IN BIOCHEMICAL SCIENCES, (2001 Nov) 26 (11) 672-8. Ref: 47
Journal code: 7610674. ISSN: 0968-0004.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20011112
Last Updated on STN: 20020125
Entered Medline: 20020109
AB The protein ***beta*** - ***catenin*** is an essential component of intercellular junctions and the Wnt growth factor signaling pathway. In many cancers, mutation of Wnt pathway components leads to activation of oncogenes by the ***beta*** - ***catenin*** -Tcf ***transcription*** ***factor*** complex. This complex is therefore an attractive target for anti-cancer drugs, but any such ***compound*** must selectively interfere with the ***beta*** - ***catenin*** -Tcf complex without disrupting other essential ***interactions*** of ***beta*** - ***catenin*** . Recent structural and biochemical studies have probed the molecular basis of ligand ***interaction*** by ***beta*** - ***catenin*** , and highlighted the possibilities and challenges of designing inhibitors of the ***beta*** - ***catenin*** -Tcf complex.

L8 ANSWER 9 OF 22 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 2001486229 MEDLINE
DOCUMENT NUMBER: 21419854 PubMed ID: 11527574
TITLE: The multifaceted roles of glycogen synthase kinase 3beta in cellular signaling.
COMMENT: Erratum in: Prog Neurobiol 2001 Dec;65(5):497
AUTHOR: Grimes C A; Jope R S
CORPORATE SOURCE: Department of Psychiatry and Behavioral Neurobiology, University of Alabama at Birmingham, Sparks Center 1057, Birmingham, AL 35294-0017, USA.
CONTRACT NUMBER: MH38752 (NIMH)
NS37768 (NINDS)
SOURCE: PROGRESS IN NEUROBIOLOGY, (2001 Nov) 65 (4) 391-426. Ref:

Journal code: [redacted]0121. ISSN: 0301-0082.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20010903
Last Updated on STN: 20020125
Entered Medline: 20011025

AB Glycogen synthase kinase-3beta (GSK3beta) is a fascinating enzyme with an astoundingly diverse number of actions in intracellular signaling systems. GSK3beta activity is regulated by serine (inhibitory) and tyrosine (stimulatory) phosphorylation, by protein complex formation, and by its intracellular localization. GSK3beta phosphorylates and thereby regulates the functions of many metabolic, signaling, and structural proteins. Notable among the signaling proteins regulated by GSK3beta are the many ***transcription*** ***factors*** , including activator protein-1, cyclic AMP response element binding protein, heat shock factor-1, nuclear factor of activated T cells, Myc, ***beta*** - ***catenin*** , CCAAT/enhancer binding protein, and NFkappaB. Lithium, the primary therapeutic ***agent*** for bipolar mood disorder, is a selective inhibitor of GSK3beta. This raises the possibility that dysregulation of GSK3beta and its inhibition by lithium may contribute to the disorder and its treatment, respectively. GSK3beta has been linked to all of the primary abnormalities associated with Alzheimer's disease. These include ***interactions*** between GSK3beta and components of the plaque-producing amyloid system, the participation of GSK3beta in phosphorylating the microtubule-binding protein tau that may contribute to the formation of neurofibrillary tangles, and ***interactions*** of GSK3beta with presenilin and other Alzheimer's disease-associated proteins. GSK3beta also regulates cell survival, as it facilitates a variety of apoptotic mechanisms, and lithium provides protection from many insults. Thus, GSK3beta has a central role regulating neuronal plasticity, gene expression, and cell survival, and may be a key component of certain psychiatric and neurodegenerative diseases.

L8 ANSWER 10 OF 22 MEDLINE DUPLICATE 8

ACCESSION NUMBER: 2001254986 MEDLINE
DOCUMENT NUMBER: 21251363 PubMed ID: 11353148
TITLE: Selective disruption of cadherin/catenin complexes by oxidative stress in precision-cut mouse liver slices.
AUTHOR: Schmelz M; Schmid V J; Parrish A R
CORPORATE SOURCE: Department of Pathology, College of Medicine, University of Arizona, Tucson, Arizona, USA.
CONTRACT NUMBER: ES09106 (NIEHS)
SOURCE: TOXICOLOGICAL SCIENCES, (2001 Jun) 61 (2) 389-94.
Journal code: 9805461. ISSN: 1096-6080.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010813
Last Updated on STN: 20010813
Entered Medline: 20010809

AB Previous work has shown that chemically induced oxidative stress disrupts the protein ***interactions*** of the ***E*** - ***cadherin*** / ***beta*** - ***catenin*** /alpha-catenin complex in precision-cut mouse liver slices (Parrish et al., 1999, Toxicol. Sci. 51, 80-86). Although these data suggest a role for oxidative stress in disruption of hepatic cadherin/catenin complexes, multiple complexes are co-expressed in the liver. Both E- and N- cadherin are co-expressed in hepatocytes, as well as ***beta*** - ***catenin*** and gamma-catenin; thus four distinct complexes mediate cell-cell adhesion in the liver: ***E*** - ***cadherin*** / ***beta*** - ***catenin*** /alpha-catenin, ***E*** - ***cadherin*** /gamma-catenin/alpha-catenin, N-cadherin/ ***beta*** - ***catenin*** /alpha-catenin, and N-cadherin/gamma-catenin/alpha-catenin. Taking advantage of the retention of normal organ architecture and cellular heterogeneity offered by precision-cut mouse liver slices,

the current study was designed to examine the impact of chemically induced oxidative stress on cadherin/catenin complexes. Precision-cut rat liver slices were challenged with diamide (25-250 microM; 6 h) or tert-butylhydroperoxide (5-50 microM; 6 h). A polyclonal antibody against beta- or gamma-catenin was used to immunoprecipitate proteins prior to Western-blot analysis with monoclonal antibodies to E- or N-cadherin. Although a decrease in ***E*** - ***cadherin*** : ***beta*** - ***catenin*** co-immunoprecipitation was seen, ***interactions*** between ***beta*** - ***catenin*** and N-cadherin were not disrupted by chemical challenge. In addition, no effect on protein ***interactions*** of gamma-catenin with either cadherin was observed. Indirect immunofluorescence was used to co-localize catenins and cadherins following chemical challenge. Consistent with the biochemical observations, a heterogeneous reduction in co-localization of ***E*** - ***cadherin*** and ***beta*** - ***catenin*** was seen in precision-cut liver slices, but not other cadherin/catenin complexes. Taken together, these data suggest that oxidative stress selectively disrupts ***E*** - ***cadherin*** / ***beta*** - ***catenin*** complexes in the liver. This response is dictated, in part, by the protein ***composition*** of the cell-adhesion complex.

L8 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:145047 CAPLUS
DOCUMENT NUMBER: 132:204001
TITLE: Method involving c-myc transcription for detection of APC pathway mutations and for drug screening
INVENTOR(S): He, Tong-Chuan; Vogelstein, Bert; Kinzler, Kenneth W.
PATENT ASSIGNEE(S): The Johns Hopkins University School of Medicine, USA
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000011195	A1	20000302	WO 1999-US18774	19990820
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6140052	A	20001031	US 1998-136605	19980820
AU 9956777	A1	20000314	AU 1999-56777	19990820
EP 1104475	A1	20010606	EP 1999-943741	19990820
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1998-136605 A 19980820
US 1997-821355 A2 19970320
WO 1999-US18774 W 19990820

AB A method for detg. the presence or absence in a cell of wild-type APC or a downstream protein in the APC transcription regulatory pathway comprises (1) introducing a Tcf-responsive reporter gene comprising upstream genomic sequences of c-myc into the cell, and (2) measuring transcription of the reporter gene. A cell which supports active transcription of the reporter gene does not have wild-type APC or a downstream protein in the APC transcription regulatory pathway. A cell contg. a mutant APC pathway may be used for drug screening. The APC tumor suppressor protein binds to .beta.-catenin, a protein recently shown to interact with Tcf/Lef transcription factors. Here, the cDNA for a gene encoding a Tcf family member that is expressed in colonic epithelium (hTcf-4) was cloned and characterized. HTcf-4 transactivates transcription only when assocd. with .beta.-catenin. Nuclei of APC-/- colon carcinoma cells were found to contain a stable .beta.-catenin-hTCF-4 complex that was constitutively active, as measured by transcription of a Tcf reporter gene. Reintroduction of APC removed .beta.-catenin from hTcf4 and abrogated the transcriptional transactivation. Constitutive transcription of TCF target

genes, caused by loss of APC function, may be a crucial event in the early transformation of colonic epithelium. It is also shown here that the products of mutant APC genes found in colorectal tumors are defective in regulating .beta.-catenin/Tcf-4 transcriptional activation. Furthermore, colorectal tumors with intact APC genes were shown to contain subtle activating mutations of .beta.-catenin that altered functionally significant phosphorylation sites. These results indicate that regulation of .beta.-catenin is crit. to APC's tumor suppressive effect and that this regulation can be circumvented by mutations in either APC or .beta.-catenin. The c-myc oncogene was identified as a target gene in the APC signaling pathway. Expression of c-myc is repressed by wild-type APC and activated by .beta.-catenin, and these effects are mediated through Tcf-4 binding sites in the c-myc promoter.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 22 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 2001043101 MEDLINE
DOCUMENT NUMBER: 20404931 PubMed ID: 10949998
TITLE: Up-regulation of E-cadherin and I-catenin in human hepatocellular carcinoma cell lines by sodium butyrate and interferon-alpha.
AUTHOR: Masuda T; Saito H; Kaneko F; Atsukawa K; Morita M; Inagaki H; Kumagai N; Tsuchimoto K; Ishii A H
CORPORATE SOURCE: Department of Internal Medicine, School of Medicine, Keio University, Tokyo, Japan.
SOURCE: IN VITRO CELLULAR AND DEVELOPMENTAL BIOLOGY. ANIMAL, (2000 Jun) 36 (6) 387-94.
Journal code: 9418515. ISSN: 1071-2690.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001207

AB Human ***E*** - ***cadherin*** is a homophilic cell adhesion molecule and its expression is well preserved in normal human hepatocytes; a decrease in its expression has been observed in poorly differentiated hepatocellular carcinoma cells. We examined the alteration of ***E*** - ***cadherin*** and catenin expressions caused by differentiation inducers in human hepatocellular carcinoma cells. Hepatocellular carcinoma cell lines, HCC-T and HCC-M, were cultured with all-trans retinoic acid (ATRA), dexamethasone (DEX), sodium butyrate, and interferon-alpha. ***E*** - ***cadherin*** expression was only up-regulated by butyrate and interferon-alpha (IFN-alpha) in both cell lines, studied by means of fluorescence immunostaining and flow cytometry. The localization of ***E*** - ***cadherin*** staining was shown at their cell membrane. According to the increase in ***E*** - ***cadherin*** expression, ***beta*** - ***catenin*** expression appeared at the cell membrane of both cell lines when treated with butyrate and IFN-alpha. Such an appearance was not observed when cells were treated with ATRA and DEX. Western blotting showed that alpha- and y-catenin expression was not changed, while only the expression of ***beta*** - ***catenin*** increased. ***Beta*** - ***catenin*** oncogenic activation as a result of amino acid substitutions or interstitial deletions within or including parts of exon 3, which has been demonstrated recently, was not detected in these cell lines by direct deoxyribonucleic acid sequencing. These results suggest that the expression and ***interaction*** between ***E*** - ***cadherin*** and wild-type ***beta*** - ***catenin*** are potentially modulated by butyrate and IFN-alpha, and that these two ***agents*** are potent inhibitors of hepatocellular carcinoma cell invasion and metastasis.

L8 ANSWER 13 OF 22 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 2000102527 MEDLINE
DOCUMENT NUMBER: 20102527 PubMed ID: 10638989
TITLE: Butyrate regulates E-cadherin transcription, isoform expression and intracellular position in colon cancer cells.
AUTHOR: Barshishat M; Polak-Charcon S; Schwartz B

CORPORATE SOURCE: Institute of Biochemistry, Food Science and Nutrition, Faculty of Agricultural, Food and Environmental Quality Sciences, The Hebrew University of Jerusalem, Rehovot, Israel.
SOURCE: BRITISH JOURNAL OF CANCER, (2000 Jan) 82 (1) 195-203. Journal code: 0370635. ISSN: 0007-0920.
PUB. COUNTRY: SCOTLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000209
Last Updated on STN: 20000209
Entered Medline: 20000131

AB Cell-to-cell adhesion, an important event in differentiation, is impaired during advanced stages of tumorigenesis. In this study, we examined the possible regulation of cell-adhesion proteins by the differentiation ***agent*** butyrate in LS174T and HM7 cells, two types of human colon cancer cells that differ in their ability to produce mucin and colonize the liver of experimental animals. The more aggressive, high-mucin-producing cell line (HM7), a clone selected from LS174T cells, showed a scattered and undifferentiated ultramorphological appearance and low basal alkaline phosphatase activity; the proteins ***beta*** - ***catenin*** and ***E*** - ***cadherin*** , as detected by immunostaining, were expressed in the cells' nuclei. All of these properties were significantly less pronounced in the less aggressive, low-mucin-producing LS174T cells. In both cell lines, butyrate treatment enhanced cell-to-cell ***interaction*** , alkaline phosphate activity, translocation of ***beta*** - ***catenin*** and ***E*** - ***cadherin*** from the nuclei to the membrane junctions, and transcription and translation of the 120-kDa ***E*** - ***cadherin*** isoform, but not of its 100-kDa isoform. Analysis of possible mechanisms of ***E*** - ***cadherin*** up-regulation revealed that butyrate induces the release of nuclear proteins from the ***E*** - ***cadherin*** promoter sequence, reducing transcription repression. We suggest that butyrate activates ***E*** - ***cadherin*** transcription through translocation of nuclear ***transcription*** ***factors*** bearing specific repressor activity. We surmise that abrogation of nuclear 100-kDa ***E*** - ***cadherin*** and ***beta*** - ***catenin*** expression following butyrate treatment is related to the control of ***E*** - ***cadherin*** gene transcription.

L8 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:549289 CAPLUS
DOCUMENT NUMBER: 131:194280
TITLE: Agents for treating cancer and other human illnesses based on .beta.-catenin
INVENTOR(S): Birchmeier, Walter; Von Kries, Jens-Peter
PATENT ASSIGNEE(S): Max-Delbrueck-Centrum fuer Molekulare Medizin, Germany
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9942481	A2	19990826	WO 1999-DE554	19990222
WO 9942481	A3	20000210		
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19909251	A1	19990826	DE 1999-19909251	19990222
EP 1054899	A2	20001129	EP 1999-913097	19990222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
JP 2002505255	T2	20020219	JP 2000-532433	19990222

PRIORITY APPLN. INFO.: DE 1998-19807390 A 19980221
WO 1999-DE554 W 19990222

AB C.beta.-catenin is a central mol. of the Wnt signal path. Increasing .beta.-catenin in the cell leads to its translocation into the cell

nucleus and to its interaction with transcription factors of the LEF-1/TCF family. This can lead to colonic cancers and melanomas (oncogenic signal path). However, .beta.-catenin also interacts with the tumor-suppressor genes APC, conductin, and E-cadherin, which have a contrary effect on the cell (antioncogenic effect). Peptides derived from LEF-1-/TCF-4 transcription factors and analogous mols. can be used in the treatment of tumors, esp. colonic cancers and melanomas. These peptides and analogous mols. influence the interaction between .beta.-catenin and LEF-1/TCF. The peptides comprise parts of the LEF-1/TCF-4 transcription factors and variants and mutations thereof, preferably the 10-40 N-terminal amino acids of LEF-1 or TCF-4, as well as peptides derived from the armadillo region of .beta.-catenin which were identified as interaction domains with LEF-1/TCF, APC, conductin, and E-cadherin. The peptides constituting interaction domains with APC or conductin can increase the concn. of .beta.-catenin in the cell. These last mols. can be used to influence the formation of tissues and organs, e.g. to promote hair growth.

L8 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:189197 CAPLUS
DOCUMENT NUMBER: 130:232471
TITLE: The protein conductin and its application for diagnosis and gene therapy of colon cancer
INVENTOR(S): Behrens, Jurgen; Birchmeier, Walter
PATENT ASSIGNEE(S): Max-Delbruck-Centrum fur Molekulare Medizin, Germany
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9911780	A2	19990311	WO 1998-DE2621	19980901
WO 9911780	A3	19990527		
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19840875	A1	19990512	DE 1998-19840875	19980901
EP 1029047	A2	20000823	EP 1998-954120	19980901
R: AT, BE, CH, DE, DK, FR, GB, IT, LI, NL, SE, FI				

PRIORITY APPLN. INFO.: DE 1997-19738205 A 19970902
WO 1998-DE2621 W 19980901

AB The invention concerns the novel protein ***conductin*** that is able to regulate the . ***beta*** .- ***catenin*** function and ***interacts*** with the tumor suppressor adenomatous polyposis coli (***APC***); and its application in the gene therapy of colon cancer. The 840 amino acid contg. protein contains domains with various activities: 78-200 is the RGS (Regulator of G-Protein Signalling) binding sequence; 343-396 is the GSK 3.beta. (glycogen synthase kinase 3.beta.) binding sequence; 397-465 is the . ***beta*** .- ***catenin*** binding sequence; 783-833 is the Dishevelled homol. region. Mutations, variants and fragments of ***conductin*** with the corresponding coding genes and mRNA sequences are also included. Antibodies and nucleic acid probes for the detection of ***conductin*** are part of the diagnosis tools. For therapeutic purposes a vector contg. the ***conductin*** gene is constructed; ***substances*** that activate and reactivate ***conductin*** in the body are co-administered, e.g. a ***substance*** that activates the ***conductin*** promoter or stabilizes mRNA. The effect of ***conductin*** was proved using SW480 cells with ***APC*** mutation and thus increased . ***beta*** .- ***catenin*** level. Introduction of ***conductin*** resulted in the decrease of . ***beta*** .- ***catenin*** to the same concn. as in non ***APC*** mutated SW480 cells. In an expt. with Xenopus embryos it was shown that ***conductin*** inhibits the Wnt/Wingless signaling pathway via its ***interaction*** with . ***beta*** .- ***catenin*** .

L8 ANSWER 16 OF 22 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 1999314752 MEDLINE
DOCUMENT NUMBER: 99314752 PubMed ID: 10408833
TITLE: Abnormal expression and function of the E-cadherin-catenin

complex in gas[redacted]c carcinoma cell lines.
AUTHOR: Jawhari A U; N[redacted] M; Farthing M J; Pignatelli M[redacted]
CORPORATE SOURCE: Digestive Diseases Research Centre, St Bartholomew's and the Royal London School of Medicine and Dentistry, Whitechapel, London, UK.
SOURCE: BRITISH JOURNAL OF CANCER, (1999 May) 80 (3-4) 322-30.
Journal code: 0370635. ISSN: 0007-0920.
PUB. COUNTRY: SCOTLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990727
Last Updated on STN: 19990727
Entered Medline: 19990715

AB Dysfunction of the cadherin-catenin complex, a key component of adherens junctions, is thought to confer invasive potential to cells. The aim of this study is to examine the expression and function of the ***E*** - ***cadherin*** /catenin complex in gastric carcinoma cell lines. Expression of ***E*** - ***cadherin*** , alpha, beta and gamma-catenin and p120ctn, and of the adenomatous polyposis coli protein (***APC***), together with function of the cadherin-catenin complex was examined in a panel of gastric carcinoma cell lines, using immunocytochemistry, Western blotting and a cell-cell aggregation assay. Protein ***interactions*** were examined by sequential immunoprecipitation and immunoblotting with antibodies to ***E*** - ***cadherin*** , alpha, beta and gamma-catenin, p120ctn and ***APC*** . Abnormalities of ***E*** - ***cadherin*** , alpha- and ***beta*** - ***catenin*** expression, were associated with disturbance of ***E*** - ***cadherin*** -catenin complex ***composition*** , loss of membranous localization and loss of calcium-dependent aggregation in six gastric carcinoma cell lines. ***APC*** protein expression and ***interaction*** with ***beta*** - ***catenin*** was preserved in five cell lines. We demonstrate frequent abnormalities of expression and function of ***E*** - ***cadherin*** and catenins, and associated disturbance of ***E*** - ***cadherin*** -mediated intercellular adhesion in gastric carcinoma cell lines. These findings support the tumour suppressor role of the ***E*** - ***cadherin*** and its contribution to the development and progression of the neoplastic phenotype in gastric carcinoma.

L8 ANSWER 17 OF 22 MEDLINE DUPLICATE 12
ACCESSION NUMBER: 1999424998 MEDLINE
DOCUMENT NUMBER: 99424998 PubMed ID: 10496679
TITLE: Chemically induced oxidative stress disrupts the E-cadherin/catenin cell adhesion complex.
AUTHOR: Parrish A R; Catania J M; Orozco J; Gandolfi A J
CORPORATE SOURCE: Department of Anesthesiology, College of Medicine, Southwest Environmental Health Sciences Center. University of Arizona, Tucson, USA.. parrish@medicine.tamu.edu
CONTRACT NUMBER: ES 06694 (NIEHS)
T3204940
SOURCE: TOXICOLOGICAL SCIENCES, (1999 Sep) 51 (1) 80-6.
Journal code: 9805461. ISSN: 1096-6080.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 19991101
Last Updated on STN: 19991101
Entered Medline: 19991015

AB The impact of xenobiotics on intercellular adhesion, a fundamental biological process regulating most, if not all, cellular pathways, has been sparsely investigated. Cell-cell adhesion is regulated in the epithelium primarily by the ***E*** - ***cadherin*** /catenin complex. To characterize the impact of oxidative stress on the ***E*** - ***cadherin*** /catenin complex, precision-cut mouse liver slices were challenged with two model ***compounds*** for the generation of oxidative stress, diamide (DA; 25-250 microM) or t-butylhydroperoxide (tBHP; 5-50 microM), for 6 h. At the concentrations used, neither ***compound*** elicited cytotoxicity, as assessed by intracellular K+

content and leakage of lactate dehydrogenase into the culture media. However, a 25% reduction in non-protein sulfhydryl levels, an indication of oxidative perturbation, was seen in liver slices treated with DA or tBHP. Total protein expression of ***E*** - ***cadherin*** , beta-, or alpha-catenin was not affected by challenge with DA or tBHP. A decrease of ***beta*** - ***catenin*** in the SDS-soluble fraction of slices, an indicator of the formation of the adhesion complex, was observed. Additionally, a decrease in ***beta*** - ***catenin*** ***interactions*** with ***E*** - ***cadherin*** and alpha-catenin, as assessed by immunoprecipitation and Western blot analysis, was seen. Disruption of the ***E*** - ***cadherin*** /catenin complex by tBHP, but not DA, correlated with enhanced tyrosine phosphorylation of ***beta*** - ***catenin*** . These results suggest that noncytotoxic oxidative stress disrupts the ***E*** - ***cadherin*** /catenin cell adhesion complex in precision-cut mouse liver slices.

L8 ANSWER 18 OF 22 MEDLINE DUPLICATE 13
ACCESSION NUMBER: 2000133658 MEDLINE
DOCUMENT NUMBER: 20133658 PubMed ID: 10668479
TITLE: Cellular mechanisms of risk and transformation.
AUTHOR: Augenlicht L H; Bordonaro M; Heerdt B G; Mariadason J; Velcich A
CORPORATE SOURCE: Department of Oncology, Albert Einstein Cancer Center, Montefiore Medical Center, Bronx, New York 10467, USA.. augen@aecom.yu.edu
SOURCE: ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (1999) 889 20-31. Ref: 59
Journal code: 7506858. ISSN: 0077-8923.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000314
Last Updated on STN: 20000314
Entered Medline: 20000302

AB Our early work using the first array and imaging methods for the quantitative analysis of the expression of 4000 cDNA sequences suggested that modulation of mitochondrial gene expression was a factor in determining whether colonic epithelial cells displayed a differentiated or transformed phenotype. We have since dissected a pathway in which mitochondrial function is a key element in determining the probability of cells undergoing cell-cycle arrest, lineage-specific differentiation, and cell death. Moreover, this pathway is linked to signaling through ***beta*** - ***catenin*** -Tcf, but in a manner that is independent of effects of the ***APC*** gene on ***beta*** - ***catenin*** -Tcf activity. Utilization of unique mouse genetic models of intestinal tumorigenesis has confirmed that mitochondrial function is an important element in generation of apoptotic cells in the colon in vivo and has demonstrated that modulation of cell death may be involved in intestinal tumor progression rather than initiation. Normal spatial and temporal patterns of cell proliferation, differentiation, and apoptosis in the colonic mucosa are determined by developmentally programmed genetic signals and external signals generated by homo- and heterotypic cell ***interactions*** , humoral ***agents*** , and lumenal contents. Mitochondrial function may play a pivotal role in integrating these signals and in determining probability of cells entering different maturation pathways. How this is accomplished is under investigation using high-density cDNA microarrays.

L8 ANSWER 19 OF 22 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:672440 CAPLUS
DOCUMENT NUMBER: 129:272659
TITLE: ***Compositions*** and methods for diagnosing/treating disease based on . ***beta*** .- ***catenin*** / ***transcription*** ***factor*** ***interactions***
INVENTOR(S): Polakis, Paul; Rubinfeld, Bonnee
PATENT ASSIGNEE(S): Onyx Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9842296	A2	19981001	WO 1998-US5416	19980318
WO 9842296	A3	19990325		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9868661	A1	19981020	AU 1998-68661	19980318
EP 970120	A2	20000112	EP 1998-914260	19980318
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002504808	T2	20020212	JP 1998-545805	19980318

PRIORITY APPLN. INFO.: US 1997-41685P P 19970324
WO 1998-US5416 W 19980318

AB Methods and compns. are described that are useful for diagnosing and/or treating disease arising from unwanted cell growth, preferably cancer, involving diagnosing cells for stabilized .beta.-catenin, or treating cells with compds. that disrupt or alter the formation of a complex consisting of .beta.-catenin/transcription factor, where the transcription factor is a member of the Lef/Tcf family. .beta.-Catenin and APC protein were analyzed in melanoma cell lines. Of the 26 melanoma cell lines examd., 8 are defective in .beta.-catenin regulation because of .beta.-catenin mutations, unusual .beta.-catenin mRNA splicing, or inactivation of APC. Transcription factor LEF1 was preferentially coimmunopptd. by anti-.beta.-catenin from melanoma cells contg. stabilized .beta.-catenin.

L8 ANSWER 20 OF 22 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:640347 CAPLUS
DOCUMENT NUMBER: 129:258971
TITLE: Interactions of .beta.-catenin, Tcf-4, and APC and the diagnosis and treatment of colorectal cancers
INVENTOR(S): Barker, Nick; Clevers, Hans; Kinzler, Kenneth W.; Korinek, Vladimir; Morin, Patrice J.; Sparks, Andrew B.; Vogelstein, Bert
PATENT ASSIGNEE(S): The Johns Hopkins University, USA; Utrecht University
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9841631	A2	19980924	WO 1998-US5506	19980320
WO 9841631	A3	19981203		
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5851775	A	19981222	US 1997-821355	19970320
US 5998600	A	19991207	US 1998-3687	19980107
AU 9867658	A1	19981012	AU 1998-67658	19980320
EP 972037	A2	20000119	EP 1998-912994	19980320
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001522234	T2	20011113	JP 1998-540832	19980320

PRIORITY APPLN. INFO.: US 1997-821355 A 19970320
WO 1998-US5506 W 19980320

AB The APC tumor suppressor protein binds to .beta.-catenin, a protein recently shown to interact with Tcf/Lef transcription factors. The gene

encoding a Tcf family member that is expressed in colonic epithelium (hTcf-4) was cloned and characterized. HTcf-4 transactivates transcription only when assocd. with .beta.-catenin. Nuclei of APC-/- colon carcinoma cells were found to contain a stable .beta.-catenin-hTCF-4 complex that was constitutively active, as measured by transcription of a Tcf reporter gene. Reintroduction of APC removed .beta.-catenin from hTcf4 and abrogated the transcriptional transactivation. Constitutive transcription of TCF target genes, caused by loss of APC function, may be a crucial event in the early transformation of colonic epithelium. It is also shown here that the products of mutant APC genes found in colorectal tumors are defective in regulating .beta.-catenin/Tcf-4 transcriptional activation. Furthermore, colorectal tumors with intact APC genes were shown to contain subtle activating mutations of .beta.-catenin that altered functionally significant phosphorylation sites. These results indicate that regulation of .beta.-catenin is crit. to APC's tumor suppressive effect and that this regulation can be circumvented by mutations in either APC or .beta.-catenin.

L8 ANSWER 21 OF 22 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:578401 CAPLUS
DOCUMENT NUMBER: 129:328962
TITLE: Studies on colon tumorigenesis and therapy using Apc knockout mice
AUTHOR(S): Taketo, Makoto M.
CORPORATE SOURCE: Laboratory of Biomedical Genetics, Graduate School of Pharmaceutical Sciences, University of Tokyo, Tokyo, Japan
SOURCE: Yakubutsu Dotai (1998), 13(3), 273-279
CODEN: YADOEL; ISSN: 0916-1139
PUBLISHER: Nippon Yakubutsu Dotai Gakkai
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review, with 44 refs., discussing the mol. genetic studies of familial adenomatous polyposis (FAP) kindreds which led to the discovery of the ***APC*** (adenomatous polyposis coli) gene on human chromosome 5q21. Mutations in ***APC*** appear to be responsible for not only FAP but also many sporadic cancers of the colorectal axis, stomach, and esophagus. The ***APC*** protein contains regions that may form an .alpha.-helical coiled-coil structure, and a sub-domain of the first 55 aa form a stable, parallel helical dimer. Antibody studies showed that the wild-type, but not mutant, ***APC*** protein is assocd. with the microtubule cytoskeleton. The predicted structure of ***APC*** , its localization, and its ***interaction*** with . ***beta*** .- ***catenin*** suggested its involvement in cell adhesion. In fact, recent studies demonstrated that ***APC*** is localized to plasma membrane sites involved in active cell migration. At the same time, . ***beta*** .- ***catenin*** ***interacts*** with hTcf-4 and Lef ***transcription*** ***factors*** , hTct-4 transactivates transcription only when assocd. with . ***beta*** .- ***catenin*** . We recently constructed a gene knockout mouse strain in which the mouse homolog of the human ***APC*** was inactivated by homologous recombination. Using this mouse strain, we elucidated the mechanism how the polyp adenomas are formed in both morphol. and genetic aspects. At the same time, we investigated the effects of carcinogens and anticancer ***agents*** on the polypsis. Accumulating evidence indicates that nonsteroidal antiinflammatory drugs (NSAIDs) reduce the incidence of colorectal cancers in human and exptl. animals, and reduce the polyp no. and size in FAP patients. Recently, evidence has been presented that COX-2 is induced in human colorectal cancers, and in the polyps of mouse FAP models. Accordingly, we inactivated the COX-2 gene in our FAP model mice, and demonstrated that both the no. and size of polyps are reduced dramatically. In addn., a COX-2 selective inhibitor caused similar results to COX-2 gene knockout mutations. These genetic and pharmacol. data open the possibility of effectively treating human FAP and various cancers with COX-2 selective inhibitors, a new class of NSAIDs.

L8 ANSWER 22 OF 22 MEDLINE DUPLICATE 14
ACCESSION NUMBER: 95255514 MEDLINE
DOCUMENT NUMBER: 95255514 PubMed ID: 7537697
TITLE: The E-cadherin complex contains the src substrate p120.
AUTHOR: Aghib D F; McCrea P D
CORPORATE SOURCE: Department of Growth and Development, University of

California, San Francisco 94143, USA.
CONTRACT NUMBER: CA 16672 (NCI)
SOURCE: EXPERIMENTAL CELL RESEARCH, (1995 May) 218 (1) 359-69.
Journal code: 0373226. ISSN: 0014-4827.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199506
ENTRY DATE: Entered STN: 19950615
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Entered Medline: 19950605

AB Using normal MDCK cells, and MDCK cells stably transfected with a temperature-sensitive viral src allele (pp60 ts-v-src), we have examined the ***composition*** and tyrosine phosphorylation of the ***E*** - ***cadherin*** complex. ***E*** - ***cadherin*** is a transmembrane calcium-dependent cell-cell adhesion molecule that is complexed with cytoplasmic proteins including alpha-catenin, ***beta*** - ***catenin*** , plakoglobin (gamma-catenin), and actin. We have identified two heterodimeric complexes which demonstrate that alpha-catenin ***interacts*** directly with ***beta*** - ***catenin*** , or with plakoglobin, in the absence of ***E*** - ***cadherin*** . ***beta*** - ***Catenin*** has previously been shown to bind directly to ***E*** - ***cadherin*** . We propose that ***E*** - ***cadherin*** associates with alpha-catenin, and thereby the actin cytoskeleton, via either ***beta*** - ***catenin*** or plakoglobin. We have further identified three new but related protein components of the ***E*** - ***cadherin*** complex, which are each cross-reactive by Western blot analysis to antibodies directed against p120, a phosphotyrosine substrate of src, and a phosphotyrosine, phosphoserine, and phosphothreonine substrate of growth factor-stimulated signaling pathways. Greater quantities of the p120-related proteins were found present in the ***E*** - ***cadherin*** immunoprecipitates of ts-src MDCK cells compared to normal MDCK cells, while two of the p120 cross-reactive species were significantly tyrosine phosphorylated in both normal and ts-src MDCK cells. The association of p120-related species with the ***E*** - ***cadherin*** complex adds them to our consideration of possible modulators of cadherin function. Likewise, the newly identified alpha-catenin- ***beta*** - ***catenin*** and alpha-catenin-plakoglobin dimers may have interesting biological properties, conceivably including the titration of catenins between cadherin and ***APC*** complexes.

=> d his

(FILE 'HOME' ENTERED AT 16:34:25 ON 20 AUG 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 16:34:59 ON 20 AUG 2002
L1 13370 S (BETA-CATENIN) OR (BETA CATENIN)
L2 55552 S LEF-1 OR TCF-4 OR APC OR CONDUCTIN OR E-CADHERIN
L3 294851 S TRANSCRIPTION FACTOR
L4 2000 S TUMOR SUPPRESSOR GENE PRODUCT
L5 6498 S L1 (P) (L2 OR L3 OR L4)
L6 1670 S L5 (P) INTERACT?
L7 75 S L6 (P) (COMPOUND OR AGENT OR SUBSTANCE OR COMPOSITION)
L8 22 DUPLICATE REMOVE L7 (53 DUPLICATES REMOVED)

=> s l8 (p) (affect? or inhibit? or promot?)
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L55 (P) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L57 (P) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L59 (P) '
5 FILES SEARCHED...
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L61 (P) '
L9 12 L8 (P) (AFFECT? OR INHIBIT? OR PROMOT?)

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L1         13370 S (BETA-CATENIN) OR (BETA CATENIN)
L2         55552 S LEF-1 OR TCF-4 OR APC OR CONDUCTIN OR E-CADHERIN
L3        294851 S TRANSCRIPTION FACTOR
L4          2000 S TUMOR SUPPRESSOR GENE PRODUCT
L5          6498 S L1 (P) (L2 OR L3 OR L4)
L6          1670 S L5 (P) INTERACT?
L7            75 S L6 (P) (COMPOUND OR AGENT OR SUBSTANCE OR COMPOSITION)
L8            22 DUPLICATE REMOVE L7 (53 DUPLICATES REMOVED)
L9            12 S L8 (P) (AFFECT? OR INHIBIT? OR PROMOT?)

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